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ON THE EFFECT OF CHLORINE ON THE FEMALE ORGANISM

[Über die Einwirkung des Chlors auf den weiblichen Organismus]

R.M. Skljanskaja, L.M. Klaus and L.M. Ssidorowa

Arch. Hyg. Bakt.
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ON THE EFFECT OF CHLORINE ON THE FEMALE ORGANISM

by

R. M. Skljanskaja, L. M. Klaus and L. M. Ssidorowa

The problem of the specific action of poisons on the female organism is of high theoretical and practical interest. Some researchers have repeatedly devoted their attention to it (1 - 16a).

A series of authors (Blum (4), Zollinger (16), Alice Hamilton (6), Lewin (10), Hirsch (8), Teleky (16a)), among others, provides data on the specific action of the following poisons on the female organism: lead, mercury, carbon monoxide, arsenic, carbon disulfide, hydrogen sulfide, phosphorus, benzene, and benzene derivatives.

The specific action of poisons on the female organism can have various expressions. Women show higher sensitivity to certain poisons, giving a higher intoxication index and more severe forms of intoxication phenomena. Sensitivity to poison shows a special increase in women during pregnancy. Some poisons change the menstrual function. Chronic action of certain poisons disturbs the course of pregnancy and leads to miscarriages, premature births, and stillbirths. Chronic injury to the parents (and particularly to the mother) by certain chemical poisons leads to weakness, infirmity, and sickliness of the offspring, and to an increase in child mortality. In chronic intoxication of the mother by some chemicals, it is possible to demonstrate the material in the amniotic fluid and in the fetal organs. Some substances also pass through the mother's milk. The character of the specific action of the poison on the female organism depends not on the isolated action on the sexual organs, but on the mechanism of action on the organism as a whole.

There has been very little research on the entire problem. Our knowledge is even less about the actual conditions in various production branches of the chemical industry.

In connection with the problem of allowing women to work in chlorine plants, we undertook a study on the effect of chlorine on the female organism.

From the literature (17 - 43) it is known that chlorine develops not only a local, but also a general action. The mechanism of chlorine action has not been explained definitively. But we know that chlorine affects metabolism, in that it disturbs oxidation processes and leads to acidosis (Sloftzoff (39, 40, 41), Lindemann (32), Minkowsky (34)). From the literature on the effects of war gases, we know that in persons poisoned with chlorine, serious changes were observed in the blood properties, with gross changes in the blood coagulability, and intravital thrombus formation in various segments of the vascular system (Podjarrissky etc.).

During our work, a second group of coworkers from our institute investigated the chlorine content of the work room. This varied considerably and, as expected, was dependent on many factors. As a rule, the chlorine content was not more than 0.0025, 0.0037, 0.004, and 0.005 mg chlorine per liter of air. In exceptional cases with disturbances, the chlorine content reached 0.011 to 0.0132 mg per liter. The work day for the chlorine workers is 6 hours, with a noon pause of ½ to 1 hour. With the chlorine concentrations usually present, stated above, use of gas masks is unnecessary. In plant failures, protective equipment is used.

Our work consisted of three parts:

1. Study of the relative sensitivity of men and women to chlorine.

In the literature, we found some data on the increased sensitivity of women to some poisons, and, in particular, the reference by Etienne Martin (33) to the increased sensitivity of women to chlorine during pregnancy. Therefore, we set up for ourselves the problem of clarifying the relative sensitivity of both sexes with respect to the systematic action of chlorine.

For this purpose, we visited one chlorine plant three times during the year 1932. There, we made a medical study of the state of health of a large group of working men and women (1).

We studied 122 persons in all: 60 men and 62 women. It must be emphasized that the average age of the male workers was higher, that they had worked longer in chlorine production, and occupied more responsible positions in the production process.

We obtained the following results:

1. The chronic action of chlorine was expressed most frequently in all those studied for the first time in diseases of the mucous membranes of the upper respiratory tract (rhinitis, laryngitis, and pharyngitis). After longer action of chlorine, there developed a tendency to atrophic processes in the mucous membranes of the upper respiratory tract.

2. In older workers who had worked longer with chlorine, the diseases of the upper respiratory tract (especially atrophic processes) and diseases of the respiratory organs, heart, and nervous system were much more frequent. In the women workers (and here we are dealing with a lower age and less total duration of working with chlorine) we found only functional heart disturbances.

3. Anemias were more frequent and of higher degree in the women workers.

4. The number of healthy persons (in respect to internal organs, nervous system, and mucous membranes of the upper respiratory tract) was much larger among the women, corresponding essentially to their younger age and shorter working time.

5. The dynamics of the health changes were more favorable in the women than in the men, also. This is likewise related to

(1) Our medical staff consisted of an internist, Dr. Travina, a neurologist, Dr. Wischnewskaja, an otolaryngologist, Dr. Pressmann, a gynecologist, Dr. Kusmin, and a hematologist.

the differences in age and working time.

6. Both the state of health in the women workers, and its dynamics, suggest to us the conclusion that the female sex is not more sensitive to the action of chlorine than is the male sex.

II. Study of the course of pregnancy and birth in women workers at chlorine plants.

To clear up the question of the course of pregnancy and birth in female chlorine workers, and the development of their offspring, we, together with Dr. Kusmin, placed all the pregnant workers in the plant under medical observation. In all, we treated 15 deliveries of female workers at the chlorine plant in the years 1932 - 33. Of these, 13 took a normal course, while 2 were premature. In one of these cases (P.) there was a macerated 4½ month fetus. In the second case, a 6½ month girl, incapable of surviving, was born to worker K. Both mothers had worked for more than a year in the chlorine plant. Worker K. stated that she had suffered a fall before the premature birth. Here, the gynecologist conjectured an unsuccessful attempt at abortion. For the worker P., trauma and infection could be excluded in the case history. The Wassermann reaction in the blood was negative. The etiology of the macerated fetus remained unclear in this case. This single case gives us no reason to relate the happening to the action of chlorine. In the other 13 cases, which ended with normal birth, the course of pregnancy ran without complications. The puerperium and lactation period also ran normally in all 13 cases. Aside from these 13 pregnancies, there were 8 other pregnancies among workers at this plant during the entire period, but we were unable to observe them. The weight of the newborn was satisfactory in most of the cases: over 3 kg in 8 cases, and below 3 kg in 4 cases. The changes of body weights in the infants could be observed only in two cases, in which the increase in weight was entirely normal (in one case, from 2,600 at birth to 5850.0 after six months; and in the other case, from 3220.0 at birth to 4970.0 after 100 days.)

Medical examinations were performed several times on 5 of the pregnant women. In three of these cases, deterioration of the state of health could be detected during pregnancy, once in the heart, in the second case, in the nervous system and mucous membranes of the upper respiratory tract; and, in the third case, a chronic bronchitis developed.

No complaints of menstrual disturbances were found. In isolated cases, we found absence of the menses for up to 19 years. But, as these women had worked for only a short time with chlorine, it was inappropriate to relate this fact to chlorine.

III. Acidosis in men and women working with chlorine, and its changes during pregnancy in the latter (2)

To reach a decision on the question of acidosis in the chronic action of low chlorine concentrations, we supplemented our clinical studies with systematic biochemical urine studies. The urine of each test subject was studied in the course of 4 days. The determinations were carried out in 24-hour portions. The urine was collected in vessels with ground stoppers, with addition of toluene. The vessels containing the urine were kept cold. As for the study methods, those suitable for volumetric analyses were used. We determined:

1. the pH – colorimetrically, according to Michaelis
2. total nitrogen – colorimetrically, according to the modification of Model
3. ammonia nitrogen – colorimetrically, according to the modification of Model
4. chloride – according to Volhard
5. oxygen deficiency – according to Müller.

(2) This part of the work was performed in consultation with Prof. Dr. Smorodinzeff.

On the basis of the data we obtained, we then calculated the ammonia coefficients and the oxidation coefficients.

A whole series of literature data (Walter (57), Mainzer (53, 54), Lichtwitz (51), Mainzer and Joffe (55), Hallerworden (46)) suggests that the excretion of ammonia increases if increased elimination of acids occurs in the organism. The urine collected in 24 hours contained an average of 0.7 g ammonia. Hasselbach has shown that the absolute amount of ammonia is subject to very strong variations and that, for this reason, the ratio of ammonia nitrogen to total nitrogen, or the so-called ammonia coefficient (from 3 to 5.8%) represents a more demonstrative value.

The degree of elimination of incompletely oxidized metabolic products can be judged from the oxidation coefficient, $\frac{\text{oxygen deficiency}}{\text{total nitrogen}}$, of Müller (if, by oxygen deficiency, we understand the amount of oxygen which is lacking for complete oxidation of the organic substance to H_2O and CO_2).

Our biochemical studies were performed on a total of 7 men and 15 women working in the chlorine plant.

In no case did the nutritional regime of the workers promote increased acidity in the organism. It was not controlled by us, but only considered. During our investigations, this regime was very monotonous. The test subjects were studied for 4 days during the working day (beginning of work at 8 A. M.). The data for the individual coefficients on all four days proved to be very closely related. Our tables always contain the averages from these four days.

Analysis of Tables 1 and 2 yields these findings: increase of the ammonia coefficients in chlorine workers (it is noteworthy that women show the same degree of this increase as men), shift of the oxidation coefficient up to the upper normal limit, and increased

TABLE 1. URINE FINDINGS FOR CHLORINE PLANT WORKMEN

Name	Diuresis	Specific Gravity	pH	Total N (grams)	NH_3-N	$\frac{NH_3\text{-}N}{N}$	Chloride (grams)	Oxygen Deficiency	Oxid. Coeff.	Viscosity	Age	Duration of work with chlorine	Job
G	1500	1015	5.4	8.316	0.769	9.30	8.67	18.12	2.17	5.1	50	30 years	Sealer
P	1284	1025	5.9	9.380	0.782	8.45	14.14	23.87	2.41	6.0	47	10	Overseer
Gr	1646	1018	6.1	10.970	0.796	7.42	13.13	16.94	1.55	4.7	28	6.5	-
F	1617	1023	5.7	14.610	1.270	8.75	16.54	22.12	1.51	4.8	24	9	Weigher
K	1812	1024	6.8	14.870	1.226	8.62	20.60	26.20	1.75	5.1	22	1¼	$CaCl_2$ unloader
Gub	1670	1022	6.3	14.450	0.828	5.61	13.95	27.92	2.30	4.9	35	8¾	Foreman
K	1552	1021	6.5	13.520	0.969	7.17	10.12	23.36	1.74	6.0	23	1¼	Shift engineer
Average				12.306	0.94	8.18	13.87	22.64	1.91	5.2			

TABLE 2. URINE FINDINGS FOR WOMEN CHLORINE PLANT WORKMEN

Name	Diuresis	Specific Gravity	pH	Total N (grams)	NH_3-N	$\frac{NH_3\text{-}N}{N}$	Chloride (grams)	Oxygen Deficiency	Oxid. Coeff.	Viscosity	Age	Duration of work with chlorine
Ssob	521	1033	5,4	7,392	0,575	7,98	4,34	10,06	1,40	5,3	23	1 yr 2 mo
Str	925	1021	5,7	9,527	0,619	6,48	7,35	12,09	1,36	4,0	18	1 yr 6 mo
J	1165	1024	5,6	7,450	0,685	9,31	9,27	12,57	1,70	—	20	5 mo
Sach	733	1011	5,5	3,771	0,373	10,12	3,12	5,94	1,57	4,0	23	2 yr
Abd	615	1025	5,7	5,800	0,522	8,92	6,10	10,04	1,86	5,2	20	1 yr 6 mo
Ssor	874	1028	5,0	8,950	0,732	8,31	9,66	15,17	1,68	5,0	22	1 yr 1 mo
P	765	1027	5,1	8,610	0,742	9,12	6,16	11,43	1,37	5,2	22	1 yr 6 mo
F	1625	1014	5,6	11,620	1,090	9,24	11,02	16,94	1,45	4,5	26	1 yr 3 mo
Sch	1783	1018	5,4	13,400	1,083	8,36	11,09	19,30	1,49	4,8	36	11 mo
N	1298	1021	5,6	11,405	0,937	8,41	12,37	15,29	1,26	5,1	20	10 mo
Star	1138	1017	5,3	8,320	0,723	8,75	7,82	9,78	1,16	4,5	22	1 yr
Schsch	1175	1024	5,7	9,700	0,648	6,68	14,48	15,54	1,65	4,3	22	1 yr
R	1000	1022	5,5	10,880	0,718	6,68	8,03	13,85	1,28	4,0	22	7 mo
Average				8,995	0,728	8,33	9,34	13,—	1,48	4,6		
					Control group							
B	1420	1023	5,6	13,10	0,726	5,5	13,24	21,38	1,65			
Na	1083	1018	6,1	10,17	0,724	7,08	8,84	12,02	1,19			
H	1250	1018	6,0	12,63	0,530	4,33	6,66	17,04	1,37			
Average				12,0	0,66	5,63	9,86	16,81	1,4			

elimination of chlorides in persons who come into strong contact with chlorine (Backmann chambers), pH shift toward the lower normal limit, and total nitrogen within the normal range.

The increase of the ammonia coefficients suggests a distinctly expressed shift in the sense of acidosis. But the organism is prepared for the increased acid formation. This is indicated by the absence of an increase in nitrogen excretion and the smallness of the shift in oxidation coefficients. It may also be commented that some men who have already worked for many years with chlorine, gave somewhat higher figures for the oxidation coefficients than did women.

To explain the stability of the shift in acid-base equilibrium, some workers were removed from the plant and taken to the clinic. Biochemical urine analyses were undertaken after ten days following their removal. In spite of the meat diet, there was a decrease in all the coefficients, and a particularly sharp decrease in the ammonia coefficient and the chloride (see Tables 3 and 4).

TABLE 3. URINE FINDINGS FOR CHLORINE PLANT WORKMEN DURING WORK.

Name	Diuresis	Specific Gravity	pH	Total N (grams)	NH_3-N	$\frac{NH_3\text{-}N}{N}$ %	Chloride (grams)	Oxygen Deficiency	Oxidation coeff.	Viscosity
G	1500	1015	5.4	8.35	0.769	9.30	8.07	18.12	2.17	5.0
Gub	1670	1022	6.3	14.45	0.828	5.61	13.93	27.92	2.30	4.9
Kal	1533	1021	6.5	13.52	0.969	7.17	10.02	23.36	1.74	6.0
S	733	1011	5.5	3.77	0.373	10.12	3.12	5.94	1.57	4.0
Average			5.8	10.0	0.734	8.05	8.03	18.83	1.94	4.9

TABLE 4. URINE FINDINGS FOR CHLORINE PLANT WORKMEN IN THE CLINIC.

Name	Diuresis	Specific Gravity	pH	Total N (grams)	NH_3-N	$\frac{NH_3\text{-}N}{N}$ %	Chloride (grams)	Oxygen Deficiency	Oxidation coeff.	Viscosity
G	2220	1017	5,8	18,74	0,886	4,76	8,94	20,87	1,11	5,7
Gub	1420	1020	6,0	15,32	0,732	4,82	7,98	23,01	1,54	4,0
Kal	1750	1016	6,3	13,34	0,936	6,85	8,78	23,04	1,63	5,1
S	1010	1007	5,8	7,66	0,466	6,15	4,84	13,04	1,70	4,1
Average			5,9	13,76	0,76	5,64	7,63	19,99	1,49	5,0

A comparison of the data obtained from women workers in the chlorine plant and the corresponding control data for 3 women working in another production branch (see Table 2) shows that the ammonia coefficient for the women in the chlorine plant is higher than in the control group, while the oxidation coefficients are equally large.

Comparison of the urine values for the pregnant and non-pregnant women in the chlorine plant (see Tables 2 and 5) shows that the ammonia coefficients are equal, while the oxidation coefficient is higher for the pregnant women. From this we can conclude that the acidosis which results from the action of chlorine does not change during pregnancy.

Comparison of the data for the pregnant women working in the chlorine plant and the control data for pregnant women working in another production branch (see Table 5) establishes that the ammonia coefficient was within the normal range in three control pregnancies, while in two other control pregnancies, there was an increase of ammonia coefficients to the same degree that could be observed in non-pregnant women workers in the chlorine plant. For these two control pregnancies, the oxidation coefficient was significantly higher than for pregnant chlorine workers. This

TABLE 5. URINE FINDINGS DURING GRAVIDITY FOR WOMEN WORKING IN THE CHLORINE PLANT AND FOR CONTROL SUBJECTS.

Name	Diuresis	Specific Gravity	pH	Total N	NH_3-N	$\frac{NH_3\text{-}N}{N}$	Chloride (grams)	Oxygen Deficiency	Oxidation Coefficient	Month of Gravidity A = work L = leave
St	985	1023	5.8	6.41	0.582	9.06	7.70	12.30	1.94	7 mo. work
P	1942	1026	5.7	12.30	0.871	7.14	14.47	18.60	1.55	5 mo. work
J	955	1012	6.7	4.86	0.394	8.20	7.96	7.92	1.62	7 mo. work
same	1508	1010	6.6	7.98	0.769	9.94	8.18	11.42	1.47	8 mo. leave
L	1238	1017	6.2	6.73	0.494	7.39	8.75	14.11	2.09	5 mo. work
same	1150	1014	6.7	5.55	0.466	8.15	7.76	8.95	1.78	7 mo. work
Average				7.3	0.596	8.31	9.3	1.22	1.74	
					Control Group					
B	1614	1015	6.9	5.31	0.461	8.85	9.20	16.08	3.08	8 mo. leave
Sch	2212	1015	6.6	8.24	0.830	10.37	11.76	26.36	3.20	8 mo. leave
S	1557	1017	6.7	8.24	0.300	5.61	8.79	18.98	2.57	6 mo. work
T	2335	1013	6.8	10.68	0.501	4.72	11.44	18.69	1.75	8 mo. leave
B	1237	1008	6.7	10.40	0.327	3.17	9.91	14.19	1.37	8 mo. leave
Average				8.57	0.483	6.14	9.0	18.9	2.39	

difference in the degree of the shift in oxidation coefficients can be explained hypothetically by saying that the women working with chlorine have become adapted to the toxic effect, so that their acid-base balance has adjusted to a certain level, and acidosis is compensated for them. The two control workers in another branch of production, who showed significant acidosis during pregnancy, were less ready for the acidotic shift, and their acidosis is less compensated, because their oxidation coefficient experienced a shift far beyond the normal range.

Other comparisons of the urine findings for women chlorine workers and control subjects before and during pregnancy and after delivery (see Tables 5 and 6) show the following: While with control subjects, who show significant acidosis during pregnancy, all the coefficients undergo a sharp drop to the norm after delivery, with women chlorine workers all these coefficients remain at the same level before and during pregnancy and after delivery. This circumstance confirms our

TABLE 6. URINE FINDINGS BEFORE GRAVIDITY AND AFTER DELIVERY FOR WOMEN CHLORINE PLANT WORKERS AND CONTROL SUBJECTS.

Name	Diuresis	Specific Gravity	pH	Total N	NH_3-N	$\frac{NH_3\text{-N}}{N}$	Chloride (grams)	Oxygen Deficiency	Oxidation coeff.	Months employment after delivery
					Before pregnancy					
St	1138	1017	5,3	8,32	0,723	8,75	7,83	9,78	1,16	
P	735	1027	5,1	8,61	0,742	9,12	6,16	11,43	1,37	
J	1165	1024	5,6	7,45	0,685	9,34	9,27	12,57	1,79	4 mo work
L	1515	1029	5,6	10,74	0,982	9,16	15,06	19,0[illegible]	1,77	2 mo leave
Average										
					Control group					
B	1540	1013	5,8	7,25	0,376	5,20	7,75	11,86	1,6	2 mo.
Sch	1510	1007	5,7	9,75	0,633	6,55	9,37	19,37	2,0	2 mo.
Average				8,5	0,50	5,87	8,02	15,61	1,8	

conclusion that the acidosis caused by chlorine does not change during pregnancy, that is, that the acidosis of pregnancy is not characterized by a chlorine acidosis.

Briefly summarized, our work shows that: Women show no higher sensitivity to the chlorine content of the air than do men. In particularly, pregnancy, delivery, puerperium, and lactation were normal, and the newborn were of normal weight.

In chlorine workers of both sexes, acidosis appeared; but it vanished some days after suspension of work. Women showed no stronger acidosis from chlorine than did men. The normal pregnancy is not influenced by chlorine. There was one premature birth in 15 pregnancies.

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